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Assessment of Antidepressant Profile of Methanolic extract of *Areca catechu* using Mice as an experimental Model

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ABSTRACT

Purpose: The purpose of present investigation to assess the anti-depressant activity of methanolic extract of *Areca catechu* using Mice model. **Methods:** The methanolic extract was prepared using cold extraction process with the help of continuous hot percolator apparatus. The final extract was evaluated for preliminary phytochemical analysis, acute toxicological studies (Mice Model). Anti-depressant assessment was carried out as per the standard methods i.e forced swimming test, tail suspension test, 5-HT induced head twitches in mice, clonidine induced aggression, L-dopa induced hyper activity and aggressive behavior test. **Results:** Results reveals that extract possess good antidepressant potential. By observing significant change in the immobility (reduced immobility) for both forced swimming test as well tail suspension test it confirms the antidepressant effect for *Areca catechu* methanolic extract. **Conclusion:** Methanolic extract of *Areca catechu* having potential antidepressant profile. Further continuing research is needed to determine constituents, those having antidepressant activity for the safe and effective use in human welfare.

Keywords: Methanolic extract, *areca catechu*, mice, immobility, tail suspension test, forced swimming.

1. INTRODUCTION

Among all neurological disorders Depression is considered to be more affective one compared to other disorders of the same class. A wide range of categories were seen from a mild to severe kinds of depression, sometimes transformed to hallucinations; cases were reported earlier (Porter et al., 2009). Depression shows typical characteristics by observing loss of appetite (anorexia), disturbance in sleep and behavior as well energy (fatigue) (Frasure et al., 2006). It was globally recognized as life threatening ailment. There is no restriction to age , it was experienced by all ages of patients from pediatrics to geriatrics (Anderson et al., 1998) Form the literature; it came to know the major categories of depression referred as unipolar and bipolar

types. 0.7 fraction cases were observed due to stressful lifestyle and shown manifestations like agitation, anxiety. 0.3 fraction known to be endogenous type (Manji et al., 2001). There were many theories reported for depression in past, widely accepted theory was monoamine theory. According to this theory, failure or hypo action of monoamine neurotransmitters at the targeted areas of brain will cause depression. In case of manic disorders it is due hyper function monoamine neurotransmitters (Miller et al., 1996). But there is no clear evidence regarding reality of proposed theory of depression as a result of neurochemical pathway of serotonin, nor epinephrine. Drugs which inhibit the reuptake of above mentioned neurotransmitters have equal efficacy for depression but due to genetic variation in the individual give variation in the drug response. Hence need personalized medication for rationality therapy. Drugs have a success rate of 0.6 as compared to desired response but many of regimens follow upto several weeks for the better patient compliance and also for obtaining good clinical outcome. We have to look after the severe secondary effects also taken into account (Ashoka et al., 2004).

Areca catechu (arecaceae/palmae) widely known as Indian nut (Joan Heller Brown et al., 2006; Pithayanukul et al., 2009; Chempakam et al., 1993; Azeez S et al., 2007). It is used in many of the therapeutic preparations from long back (Ancient Times). It is also useful for digestion after meals as an Indian culture. The chief constituents show styptic property, carminative effect. It is rich of tannins, pyrogallol, and volatile constituents (oil) along with alkaloids namely arecaidine, guvacoline, arecoiline, guyacine which exhibit parasympathomimetic effect. Literature also confirms they possess euphoric, anti-depressant, stimulant, anti-ulcer, hepato protective, antifertility, hypoglycemic effects (Kafle Sajala et al., 2011; Shrestha et al., 2010; Boucher et al., 2002).

An attempt was performed to investigate the antidepressant potential of methanolic extract of *Areca catechu* by performing forced swinmed test, tail suspension test (Mice Model). Evaluate the effect of areca catechu on behavioral models like 5-HT induced head twitches in mice, clonidine induced aggression; L-dopa induced hyper activity and aggressive Model.

2. MATERIALS AND METHODS

2.1. Materials

The present research investigation was performed after the clearance from institutional animal ethics committee (IAEC) of M.A.M College of Pharmacy, Andhra Pradesh (1987/PO/Re/S/17/cpcsea.Exp.No.7).

Chemicals used were procured from commercial lab (AR), details include methanol, 0.9% Sodium Chloride solution from Aman scientific Hyderabad. Pure samples like Imipramine, 5-HT, Lorazepam, Clonidine were got as complementary sample from Meditech Pharma pvt Ltd, Baddi.

2.2. Cold Extraction

Cold Extraction process was chosen to prepare methanolic extract of *Areca catechu*. 200 gm of Indian nut powder was transferred to Extractor (container) and soaked in Methanol for a week shake the contents with the help of shaking apparatus (agitator). After 7 days the mixture was subjected to straining by using clean cotton wool.

5 week male mice's were chosen as experimental model for conducting the present research investigation. They weigh on average 50 ± 10 gm were housed in a cage, each cage containing four animals were preserved at ambient strict conditions for a week; temperature maintained at $27\pm3^\circ\text{C}$ with 1:1 ratio of light: Dark for every 12 hour cycle. This conditions were maintained a week to get accusative to the environment. During this period animals fed with standard diet along with *ad libitum*.

2.3. *In-vivo* models of Depression

2.3.1. Forced Swimming Test:

Glass cylinder with a dimension of $45\times20\text{ cm}^2$ were collected they were cleaned and kept a side. Place the animal on cylinders containing water at a depth of 38 cm, due to this animals were unable to touch their bottom. Temperature maintained constant throughout the test at $25\pm2^\circ\text{C}$. 2 swimming sessions were carried out as per the standard procedure (Porsolt et al., 1977).

2.3.2. Tail Suspension Test:

Animals were suspended on the edge of table about a height of 50 cm from the ground. Adhesive tape was placed nearly 1 cm from the tip of the tail. The immobility time was noted during the minimum test period of 6 min. when there was no mobility or movement of body when hanged passively is considered to be Immobile. Doses were administered as per the procedure demonstrated by Shashikumara et al., (2017).

2.3.3. 5-HTP induced head twitches:

After administering the standard and test drugs, Animals were treated with 5-HTP at a level of 100 mg/kg via ip route. The head twitches was observed after the administration of 5-HTP. The number of twitches was counted by staggering method as per procedure explained by Vijaya Kumar et al., (2016).

2.3.4. Clonidine induced aggression:

Clonidine was given 1 h after the administration of the test and standard drugs. The animals were then caged in bell shaped glass jar with a floor area of approximate 16 cm². The biting/fighting episodes were recorded live by a blind observer over a period of 30 min, in each pair.

2.3.5. L-DOPA induced aggression, hyperactivity:

L-DOPA was given 1 h after the administration of the test and standard drugs, Stages of activity and aggressive behavior were recorded live every 10 min for 30 min after L-DOPA administration by the blind observer. The different parameters of observation were piloerection, salivation, increase in motor activity, irritability, reactivity, jumping squeaking, and aggressive fighting.

2.4. Statistical Analysis:

Results were expressed as mean ± S.E.M. Statistical analysis was performed using one-way analysis of variance (ANOVA). If $P < 0.05$ statistically significant.

3. RESULTS AND DISCUSSION

% yield for methanolic extract of *Areca catechu* was founded as 25.2%. Results for primary phytochemical screening reveal the presence of flavonoid, alkaloids, saponins, phenols, steroids, tannins in methanolic extract of *Areca catechu*. Results for forced swimming test; the significant change in the immobility was reveals the extract possessing good anti-depressant property and the same confirmed from the results of tail suspension test (significant fall in the immobility). Data for FST, TST was presented as Table 1-2 and the same was represented as Fig. 1-2 respectively.

Results for 5-HTP induced twitches; significant increase in twitches to control group and it was found more effective for high dose extract (400 mg/kg), it was also found that the same group more effective than other doses as well imipramine also. Data was summarized as table 3 and the same was presented as Fig 3. Results for L-DOPA induced hyper activity and aggression behavior model; significant increase in the aggressive behavior for all extractive compounds compared to control groups. Data was presented as table 4, Fig.4. Results for Clonidine induced aggression; significant increase in the latency to first attack and decrease the no. of bouts compared to control. Data was summarized in table 5, presented as Fig.5.

Table 1: Forced Swim Test

Group	Treatment (mg/kg)	Immobility Time (sec)
I	Control	147.40±5.59
II	MEAC-100	134.70±5.62
III	MEAC-200	116.85±4.84'
IV	MEAC-400	101.80±4.95'
V	Imipramine-15	83.30±7.00'

Values expressed Mean ± SD n=6; * = P<0.001; MEAC- Methanolic Extract of *Areca catechu*

Table 2: Tail Suspension Test

Group	Treatment (mg/kg)	Immobility Time (sec)
I	Control	196.10±12.11
II	MEAC-100	171.45±7.8*
III	MEAC-200	150.05±6.38*
IV	MEAC-400	108.05±4.46*
V	Imipramine-15	87.85±4.01*

Values expressed Mean ± SD n=6; * = P<0.01; ** = P<0.001

Table 3: 5-HTP Induced Twitches

Group	Treatment (mg/kg)	Head twitches
I	Control	13±1
II	MEAC-100	21±2*
III	MEAC-200	29±3**
IV	MEAC-400	38±4**
V	Imipramine-15	24±2**

Values expressed Mean ± SD n=6; * = P<0.01; ** = P<0.001

Table 4: L-DOPA-induced hyperactivity and aggressive behavior

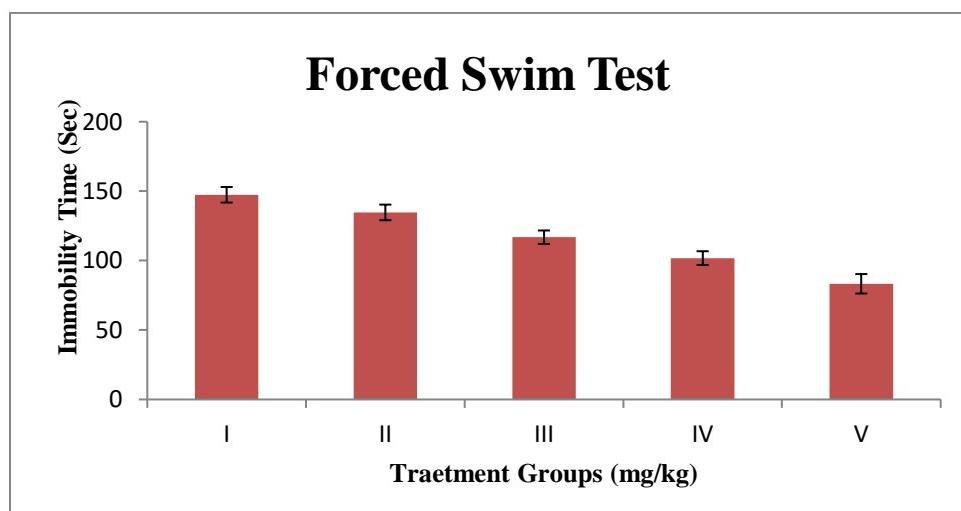
Group	Treatment (mg/kg)	Behavioural Score
I	Control	0.9
II	MEAC-100	2.1±0.2*
III	MEAC-200	2.1±0.2*
IV	MEAC-400	2.5±0.2*
V	Lorazepam-2.5	2.05±0.2*

Values expressed Mean ± SD n=6; * = P<0.01; ** = P<0.001

Table 5: Clonidine induced aggression

Group	Treatment (mg/kg)	% Response	
		Latency	Fighting
I	Control	101.9±10.1	100.5±8.3
II	MEAC-100	121.4±12.1*	89.9±8.9*
III	MEAC-200	131.1±13.1**	68.3±6.8**
IV	MEAC-400	132.8±9.5**	65.4±6.3**
V	Lorazepam-2.5	139.98±8.1**	42.8±4.3**

Values expressed Mean ± SD n=6; * = P<0.01; ** = P<0.001

**Fig.1 Forced Swim Test**

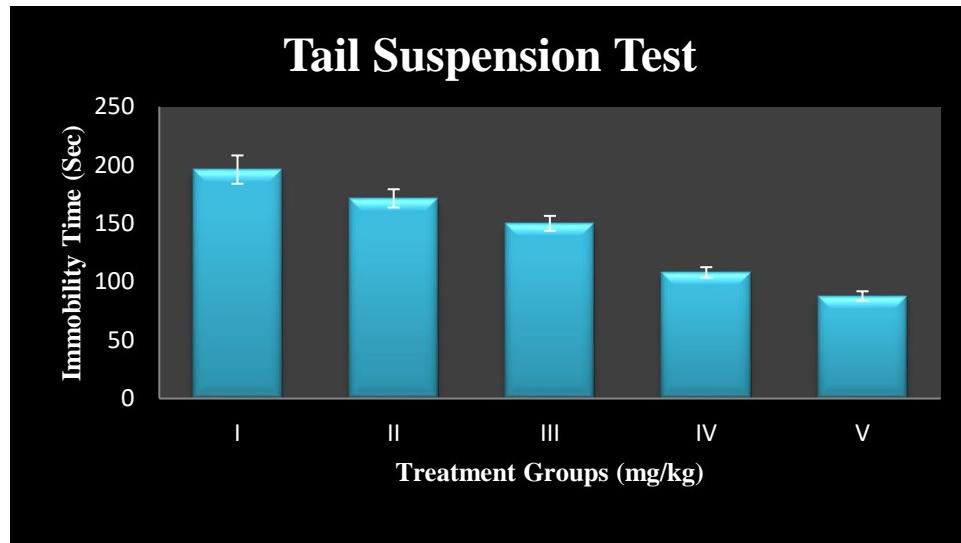


Fig.2 Tail Suspension Test

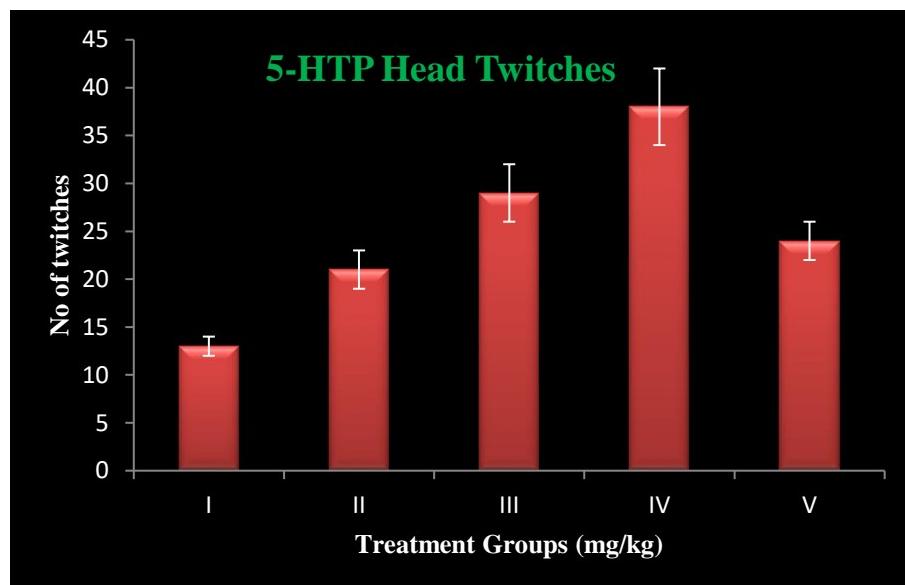


Fig.3 5-HTP Head Twitches

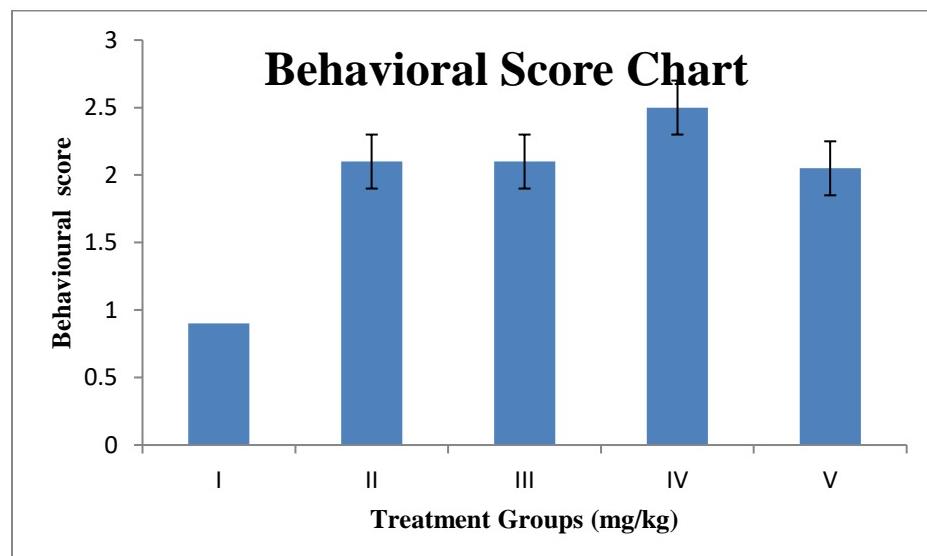


Fig.4 Behavioral Chart (L-DOPA-induced hyperactivity and aggressive behavior)

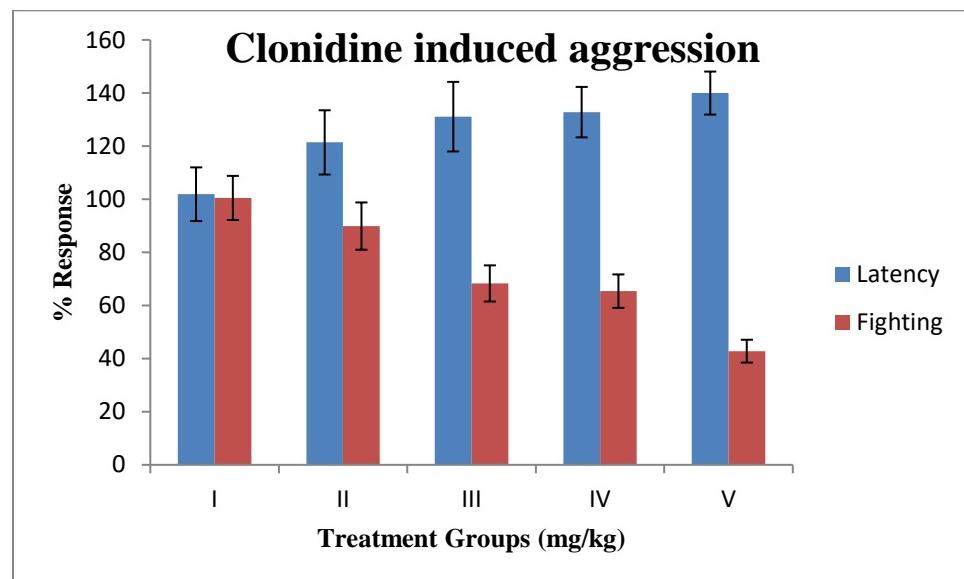


Fig.5 Clonidine induced aggression chart

The reduction in the dose of stand treating drug for any disease or disorder is the essential criterion for pharmaceutical scientist. To provide better, safe, efficacious drug delivery is another challenge for Rationality of treatment for prescriber as well all health care team. Future prospective of this current investigation was to isolate and identify the phytochemical, which shows the desired anti-depressant profile.

4. CONCLUSION

The current research investigation proves the antidepressant potential for methanolic extract of Areca catechu in all behavioral experimental models using mice such as Forced Swimming Test, Tail Suspension Test, 5-HTP induced twitches, L-DOPA induced hyperactivity and aggression, Clonidine induced aggression. Further investigations required to know the exact mode of action and also to identify the phytochemical moiety responsible for antidepressant profile.

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Conflict of Interest:

The authors declare that there are no conflicts of interests.

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This study has not received any external funding.

Ethical approval

The Animal ethical guidelines are followed in the study for experimentation. The present research investigation was performed after the clearance from institutional animal ethics committee (IAEC) of M.A.M College of Pharmacy, Andhra Pradesh (1987/PO/Re/S/17/cpcsea.Exp.No.7).

Data and materials availability:

All data associated with this study are present in the paper.

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